

JUDGE SWAIN

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF NEW YORK

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GE HEALTHCARE BIO-SCIENCES AB, GE
HEALTHCARE BIO-SCIENCES
CORPORATION, and
GENERAL ELECTRIC COMPANY,

Plaintiffs,

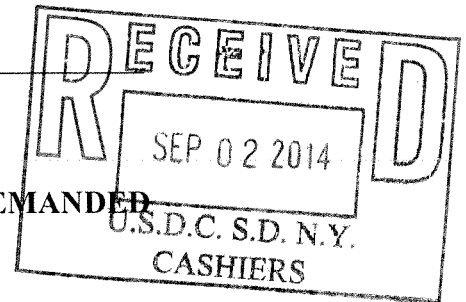
v.

BIO-RAD LABORATORIES, INC.,

Defendant.

Civil Action No. _____

JURY TRIAL DEMANDED



COMPLAINT

Plaintiffs GE Healthcare Bio-Sciences AB, GE Healthcare Bio-Sciences Corporation, and General Electric Company (together, “GE”), by their attorneys, bring this civil action for patent infringement against Defendant Bio-Rad Laboratories, Inc. (“Bio-Rad”), and allege as follows:

NATURE OF THE ACTION

1. GE brings this action to seek damages and injunctive relief arising out of the infringement by Bio-Rad of U.S. Patent No. 8,821,718 (the “‘718 patent,” attached hereto as Exhibit A), entitled “Automated Fluid Handling System” (“the Patent-In-Suit”).

PARTIES

2. Plaintiff GE Healthcare Bio-Sciences AB (“Bio-Sciences AB”) is a Swedish company, based in Uppsala Sweden, and is a subsidiary of Plaintiff General Electric Company.

3. Plaintiff GE Healthcare Bio-Sciences Corporation (“Bio-Sciences Corp.”) is a Delaware corporation, with a principal place of business in New Jersey, and is a subsidiary of Plaintiff General Electric Company.

4. Plaintiff General Electric Company is a New York corporation, with a principal place of business at 3135 Easton Turnpike, Fairfield, Connecticut 06828, and controls and is the ultimate parent company of Bio-Sciences AB and Bio-Sciences Corp.

5. Bio-Sciences AB is the assignee and owner of the '718 patent. On September 2, 2014, Bio-Sciences AB granted Bio-Sciences Corp. a royalty-free exclusive license to sell products in the United States under the '718 patent.

6. Defendant Bio-Rad is a publically-traded corporation incorporated under Delaware law, with a principal place of business located at 1000 Alfred Nobel Drive, Hercules, California.

JURISDICTION AND VENUE

7. This Court has subject matter jurisdiction over GE's claims under 28 U.S.C. §§ 1331 and 1338(a) because the claims arise under the United States Patent Laws, 35 U.S.C. § 1 *et seq.*

8. This Court has personal jurisdiction over Bio-Rad because Bio-Rad regularly and systematically transacts business in this District.

9. Venue is proper in this District under 28 U.S.C. §§ 1391(b) and (c) and 1400(b) because, on information and belief, Bio-Rad has committed, and intends to commit, acts of infringement in this District.

BACKGROUND

10. Plaintiff Bio-Sciences AB is a leading developer, manufacturer, and supplier of biopharmaceutical manufacturing technologies dedicated to helping customers deliver better healthcare to people around the world. It provides expertise and tools to support research of cells, proteins and drug discovery, and equipment to support large-scale manufacturing of

biopharmaceuticals. One important line of products developed by Bio-Sciences AB is its protein purification systems, including products marketed and sold under the trade name ÄKTA™.

11. Protein purification is an important aspect of biopharmaceutical research and manufacturing. Purification is a series of processes intended to isolate a single or small number of proteins from a complex mixture, which is essential for the characterization of the function, structure, and interactions of proteins of interest. Protein purification can be roughly divided into an analytical and preparative method: the analytical method aims to detect and identify proteins in a mixture, while the preparative method aims to produce large quantities of proteins for purposes such as industrial use and typically involves chromatography.

12. Bio-Sciences AB has been developing, manufacturing and selling innovative protein purification-related technologies since the 1950s.

13. Beginning in or about 2003, Bio-Sciences AB began developing a modular design for protein purification systems to enable researchers to more quickly, easily, and cost-effectively purify proteins. This modular design provides a system that not only simplifies researchers' work, but also gives researchers a flexible option for expanding and tailoring their purification capabilities as the research progresses.

14. Bio-Sciences AB's modular protein purification systems include its ÄKTA systems, which offers a range of chromatography systems for fast purification of proteins and other molecules from microgram to kilogram levels of target product. The ÄKTA pure and ÄKTA avant systems, for example, include a distinctive modular system design that offers a large range of options to allow flexibility in purification of proteins. The ÄKTA pure system, for example, is customizable, meaning it can be easily tailored to the researcher's precise needs through a broad selection of hardware options from valves and tubing to monitors and fraction

collectors. Among other things, this system also provides for separation of fluidics sections (external to the housing) from non-fluidics sections (internal to the housing).

15. Bio-Sciences AB's user-friendly modular protein purification systems were groundbreaking when they were first introduced, and have been greeted with considerable praise. In fact, when the ÄKTA avant system was first launched in 2009, it was the first chromatography system on the market to offer a flexible modular design that included, for example, an attractive panel design separating the fluidics section from the non-fluidics section. Thereafter, Bio-Sciences AB expended considerable effort and expense to further develop the design and launched the ÄKTA pure system in 2012. The year after, the ÄKTA pure system was nominated as the best new separations product introduced on the market in 2012 by SelectScience, an independent, expert-led scientific review resource for the worldwide scientific community.

16. Bio-Sciences AB develops, manufactures and sells the ÄKTA pure and ÄKTA avant systems. General Electric Company markets and sells the ÄKTA pure and ÄKTA avant systems throughout the world, including through its Bio-Sciences Corp. subsidiary in the United States.

GE's Patents

17. Bio-Sciences AB has made significant investments in the research, development, and testing of preparative protein purification systems, including the technology embodied by the ÄKTA protein purification systems.

18. To protect those investments, Bio-Sciences AB applied for and obtained a number of patents, including the '718 patent.

19. The '718 patent was duly and legally issued by the United States Patent and Trademark Office ("USPTO") on September 2, 2014 to Johan Blomberg and Mats Lundkvist,

after full and fair examination, for an “Automated Fluid Handling System.” The ’718 patent was originally assigned to Bio-Sciences AB.

20. On September 2, 2014, Bio-Sciences AB granted Bio-Sciences Corp. a royalty-free exclusive license to, among other things, use, offer for sale and sell products practicing the ’718 patent in the United States.

Bio-Rad’s Infringing Activities

21. In January 2013, Bio-Rad unveiled a suite of protein purification systems, including the Next Generation Chromatography (“NGC”) system. Bio-Rad advertised the NGC system as including a modular design that allowed users to customize and modify the system based on their changing needs. In fact, this modular design is copied from the ÄKTA avant system and looks strikingly similar to the ÄKTA pure system. On information and belief, Bio-Rad used GE’s ÄKTA system in the design of the NGC system and intentionally designed the NGC to resemble the design of GE’s products, particularly the modular features of the ÄKTA avant and ÄKTA pure systems covered by the ’718 patent claims.

22. When Bio-Rad launched the NGC system in 2013, it underscored the value of a modular design, which Bio-Rad advertised allowed for greater flexibility and user-friendliness. Although Bio-Rad emphasized the innovative nature of its modular design, it was well aware that GE had had a modular design for a protein purification system on the market since 2009.

23. Bio-Rad specifically targeted existing and potential ÄKTA customers as part of its campaign to sell its NGC systems.

24. Bio-Rad is infringing the ’718 patent by making, using, providing, offering to sell, and selling (directly or through intermediaries) the NGC, in this district and elsewhere in the United States and abroad.

INFRINGEMENT OF U.S. PATENT NO. 8,821,718

25. GE repeats and realleges each and every allegation set forth in the preceding paragraphs as if fully set forth therein.

26. Bio-Rad is presently making, using, offering for sale, and/or selling a system for preparative protein purification (including, without limitation, the NGC system) that infringes one or more claims of the '718 patent, literally or under the doctrine of equivalents.

27. Such activities by Bio-Rad as described above violate one or more subsections of 35 U.S.C. § 271.

28. GE has suffered economic harm as a result of Bio-Rad's infringing activities in an amount to be proven at trial.

29. Bio-Rad's activities have caused and will continue to cause GE irreparable injury for which there is no adequate remedy at law, unless Bio-Rad's infringing activities are enjoined by this Court under 35 U.S.C. § 283.

DEMAND FOR JURY TRIAL

GE hereby demands a trial by jury on all issues so triable.

PRAYER FOR RELIEF

WHEREFORE, GE respectfully requests that this Court:

1. Enter judgment in favor of GE on each of its claims;
2. Enter judgment against Bio-Rad adjudging the Patent-In-Suit to be valid, enforceable, and infringed;
3. Issue a preliminary and permanent injunction against Bio-Rad for infringement of the Patent-In-Suit;

4. Award GE an amount adequate to compensate for Bio-Rad's infringement of the Patent-In-Suit, including a reasonable royalty and lost profits under 35 U.S.C. § 284;
5. Declare that this is an exceptional case under 35 U.S.C. § 285 and award GE its attorneys' fees and costs incurred in prosecuting its claims; and
6. Award such other relief as this Court deems proper.

Dated: September 2, 2014

Respectfully submitted,



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General Electric Company

Exhibit A



US008821718B2

(12) **United States Patent**
Blomberg et al.

(10) **Patent No.:** **US 8,821,718 B2**
(45) **Date of Patent:** **Sep. 2, 2014**

(54) **AUTOMATED FLUID HANDLING SYSTEM**

USPC **210/85**; 210/656; 210/348; 210/198.2;
210/97; 422/67; 422/509; 211/188; 137/343

(75) Inventors: **Johan Blomberg**, Uppsala (SE); **Mats Lundkvist**, Uppsala (SE)

(58) **Field of Classification Search**

None

See application file for complete search history.

(73) Assignee: **GE Healthcare Bio-Sciences AB**, Uppsala (SE)

(56) **References Cited**

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

U.S. PATENT DOCUMENTS

4,125,464 A * 11/1978 Burger et al. 210/658
4,224,033 A * 9/1980 Hansen et al. 436/53
5,766,460 A 6/1998 Bergstrom et al.
5,792,742 A * 8/1998 Gold et al. 514/9.3
6,190,617 B1 * 2/2001 Clark et al. 422/562
6,599,484 B1 * 7/2003 Zigler et al. 422/130
7,374,674 B2 5/2008 Miyauchi et al.

(Continued)

FOREIGN PATENT DOCUMENTS

WO WO 00/22429 4/2000
WO WO 2006/134035 12/2006

OTHER PUBLICATIONS

EP Office Action Dated Feb. 26, 2014 Issued on Corresponding EP Application No. 10786454.8.

(Continued)

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(30) **Foreign Application Priority Data**

Jun. 9, 2009 (SE) 0950431

(51) **Int. Cl.**

B01D 35/00 (2006.01)
B01D 35/22 (2006.01)
B01J 10/00 (2006.01)
A47B 47/00 (2006.01)
G01N 30/88 (2006.01)
G01N 35/00 (2006.01)

(52) **U.S. Cl.**

CPC **G01N 30/88** (2013.01); **G01N 2030/8881** (2013.01); **G01N 2035/00326** (2013.01)

Primary Examiner — Nam Nguyen

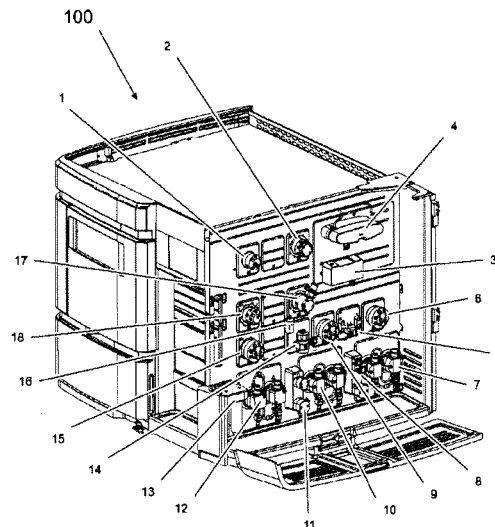
Assistant Examiner — Richard Gurtowski

(57)

ABSTRACT

Automated fluid handling system comprising a housing (20) and two or more fluid handling units (26) arranged as interchangeable modular components with an external fluidics section (30) and an internal non fluidics section (32), and wherein the housing (20) comprises a liquid handling panel (22) with two or more of component positions for receiving said interchangeable modular components (26) such that the external fluidics section (30) is separated from the non fluidics section (32) by the liquid handling panel (22).

18 Claims, 10 Drawing Sheets



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(56)

References Cited

U.S. PATENT DOCUMENTS

2002/0185442 A1 12/2002 Maiefski et al.
2004/0089057 A1 5/2004 Hobbs et al.
2008/0035542 A1 2/2008 Mourtada et al.

2008/0233653 A1 * 9/2008 Hess et al. 436/43

OTHER PUBLICATIONS

JP Office Action Dated Dec. 17, 2013 Issued on Corresponding JP
Application No. 2012-514920.

* cited by examiner

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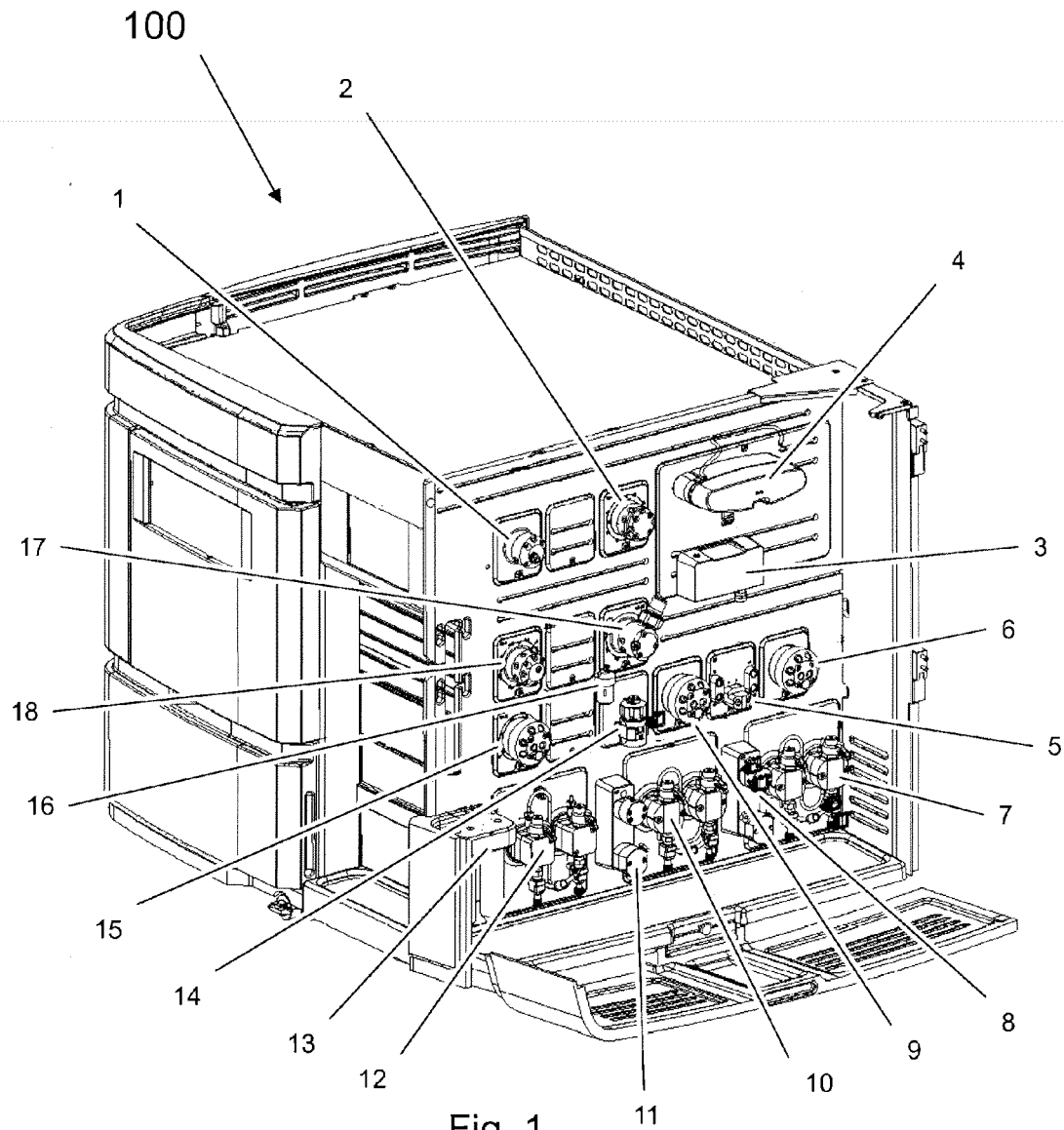


Fig. 1

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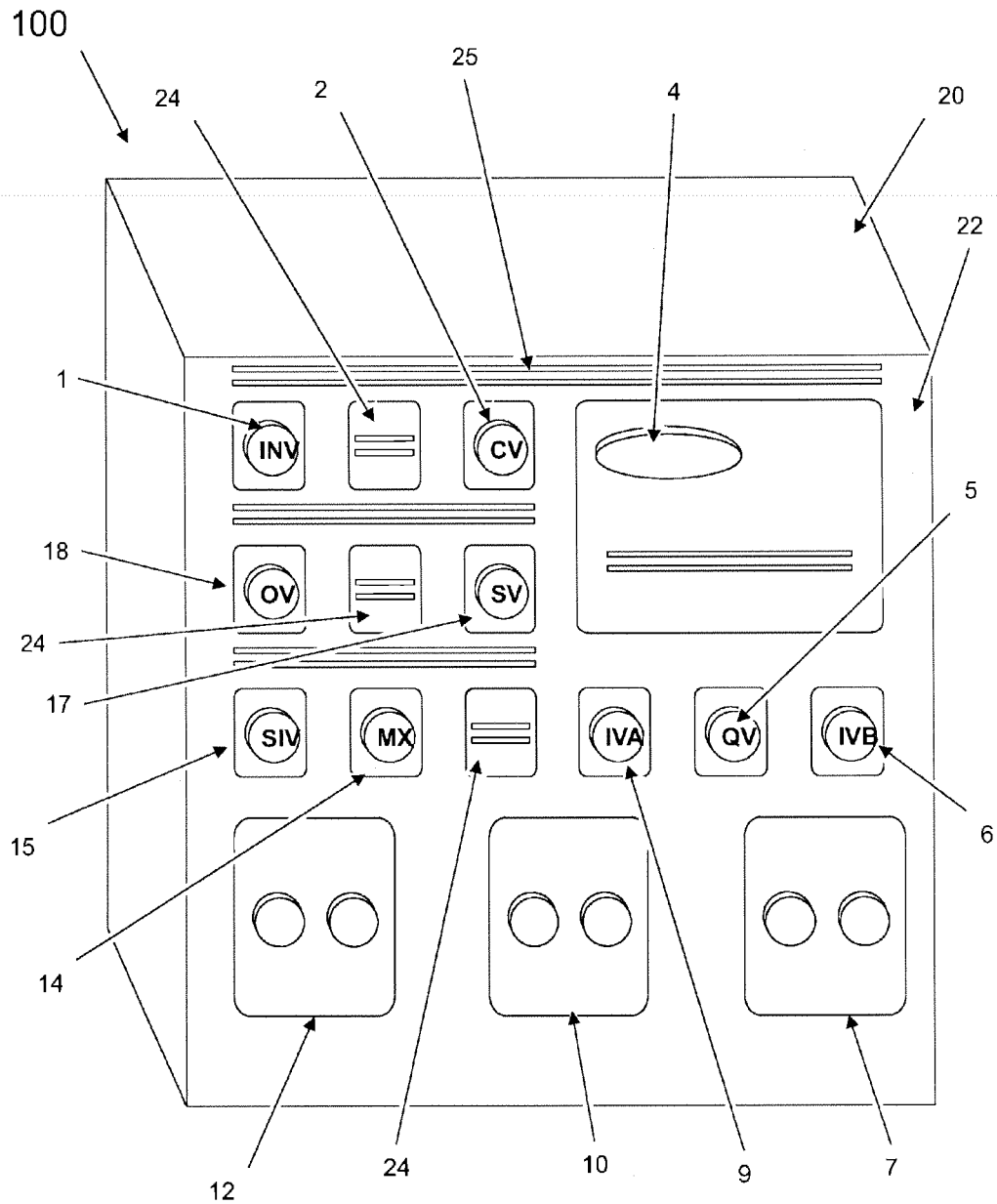


Fig. 2

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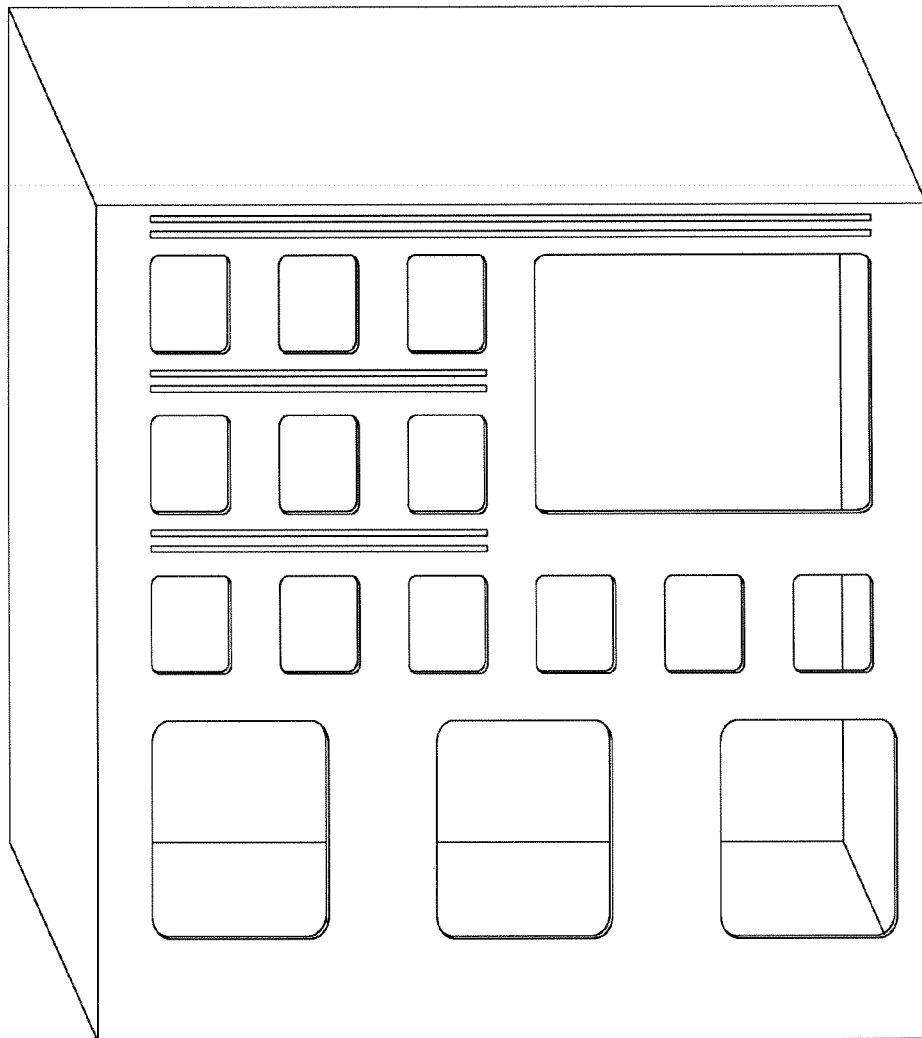


Fig. 3

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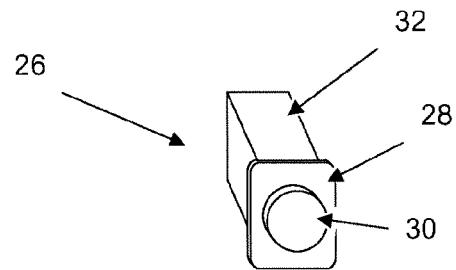


Fig. 4a

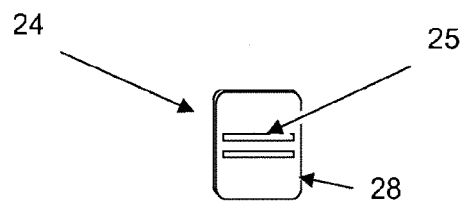


Fig. 4b

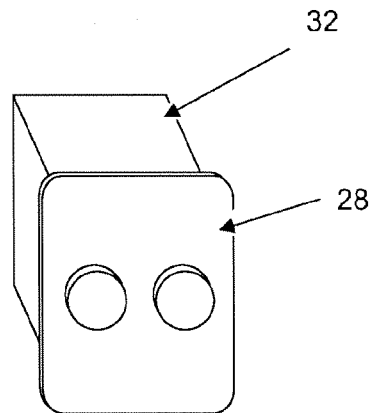


Fig. 4c

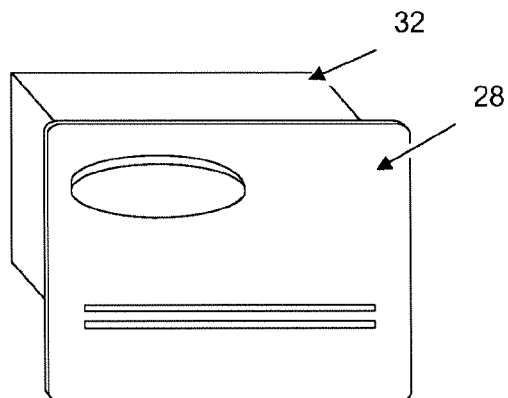


Fig. 4d

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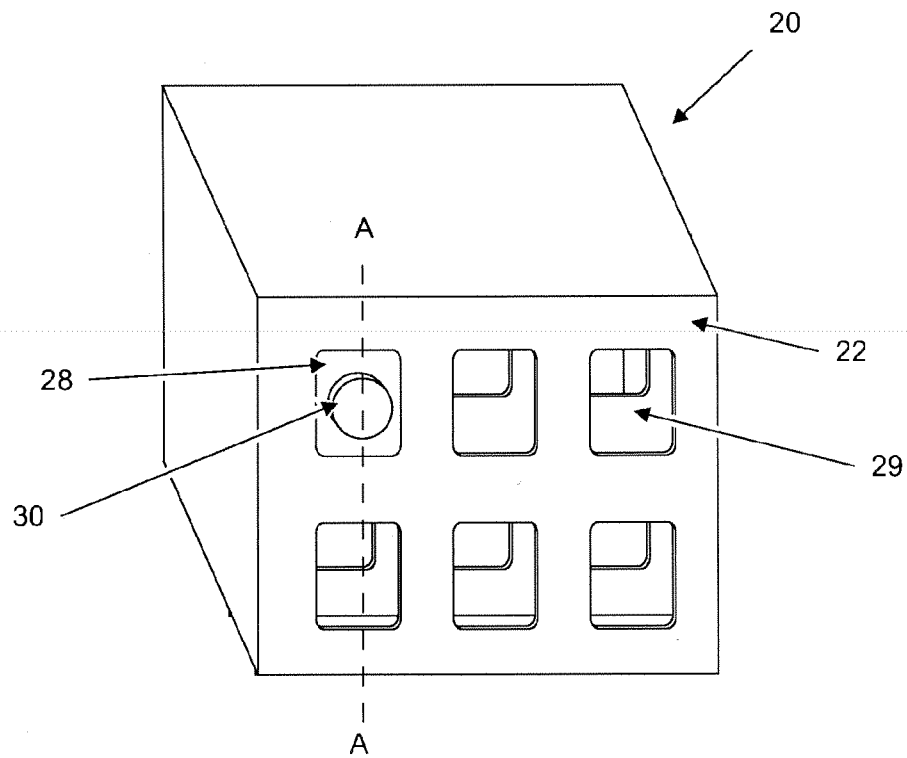


Fig. 5a

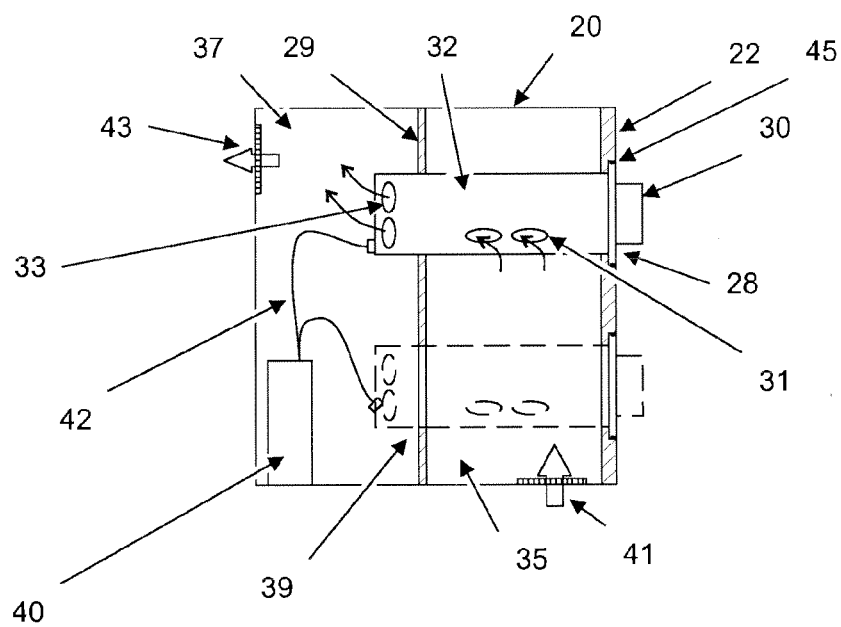


Fig. 5b

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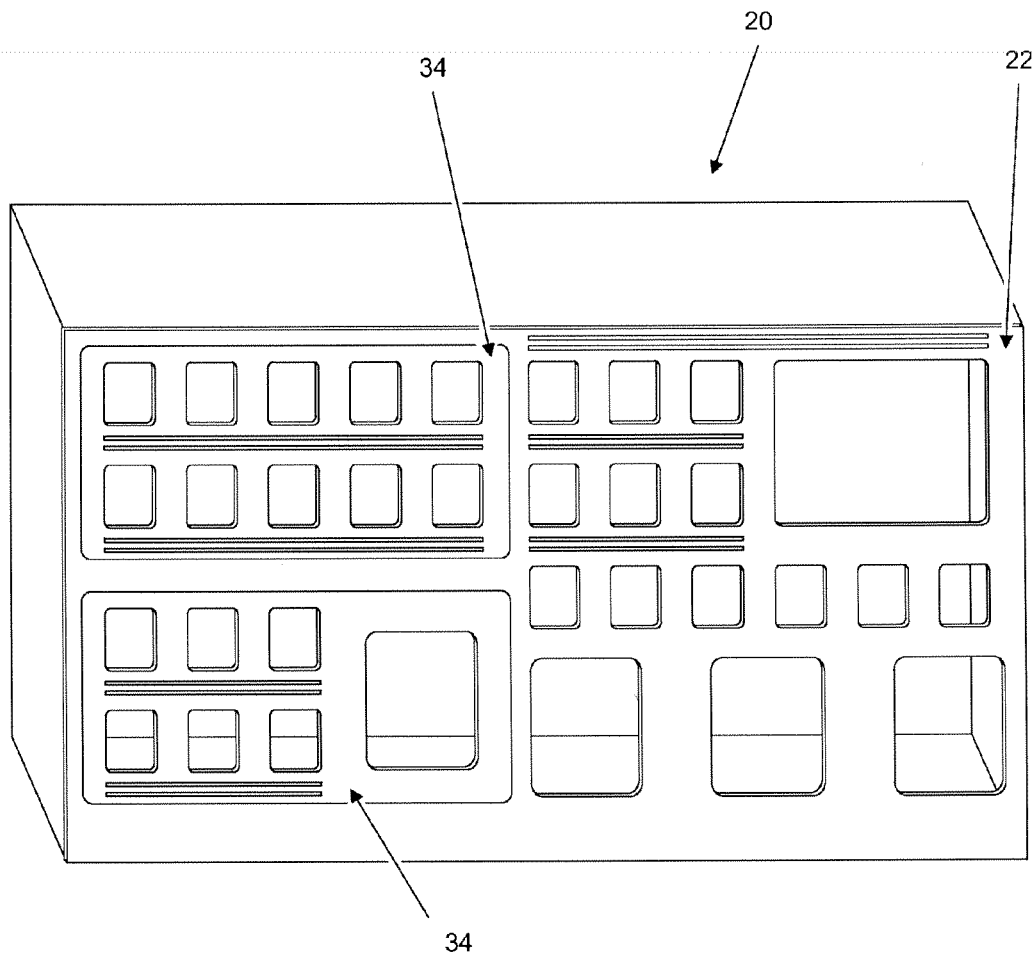


Fig. 6

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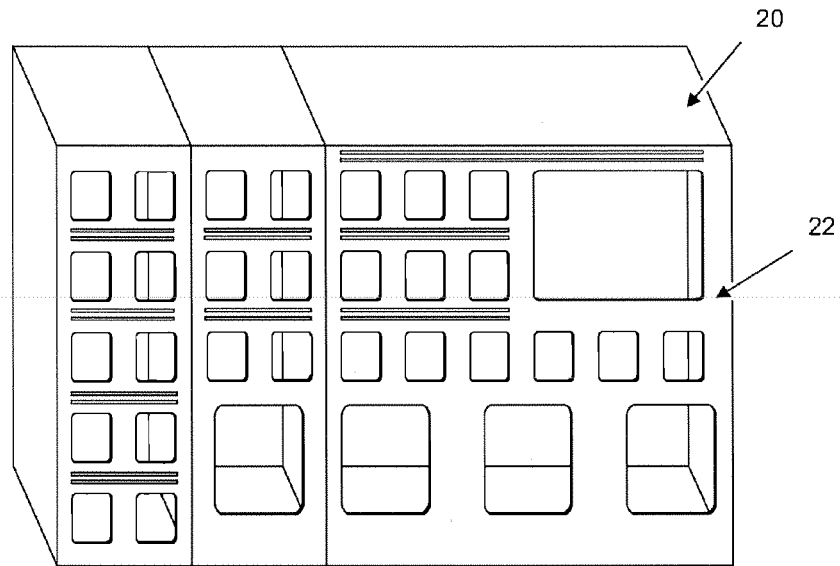


Fig. 7a

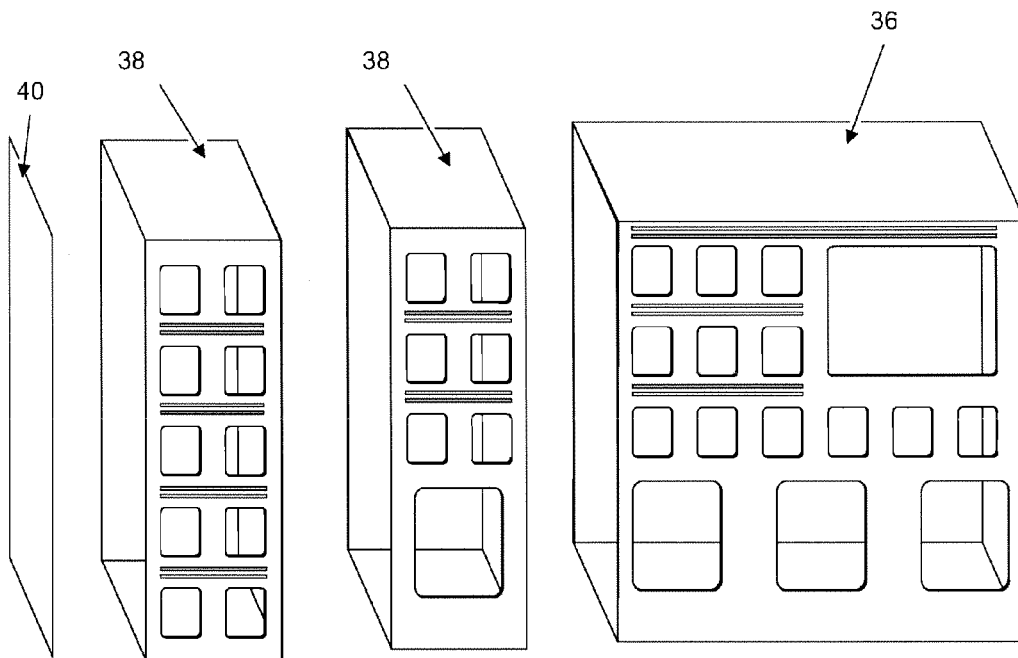


Fig. 7b

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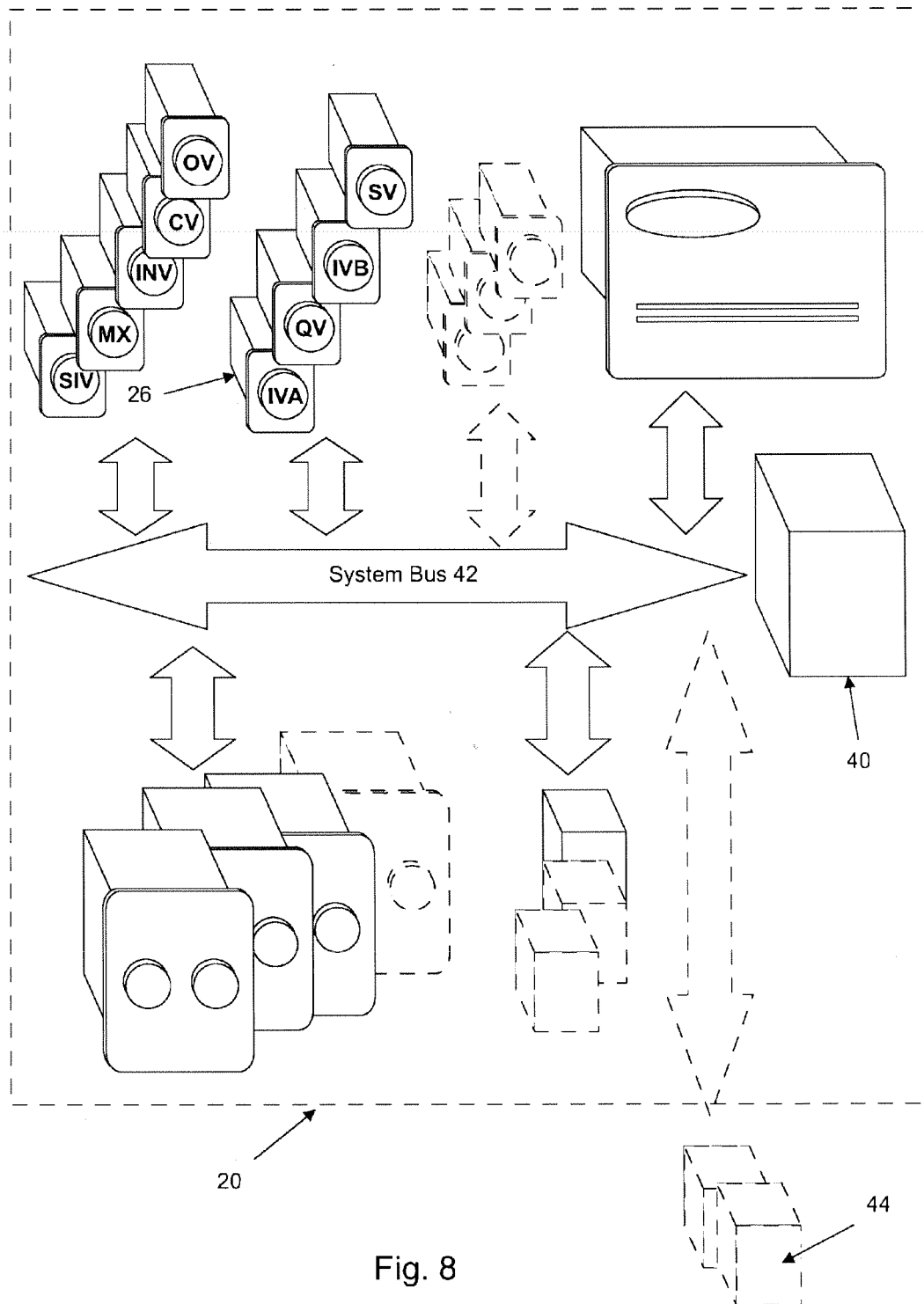


Fig. 8

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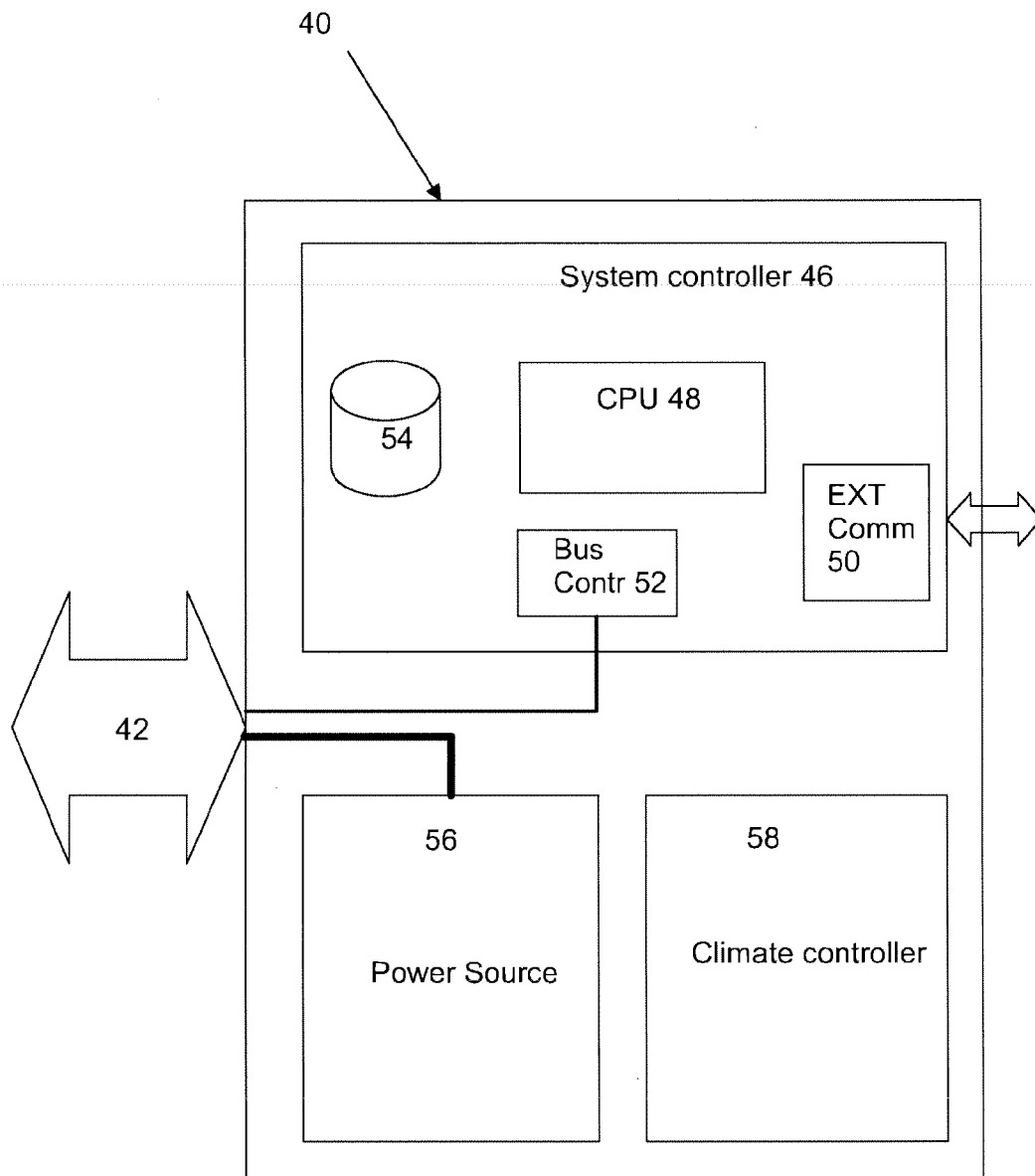


Fig. 9

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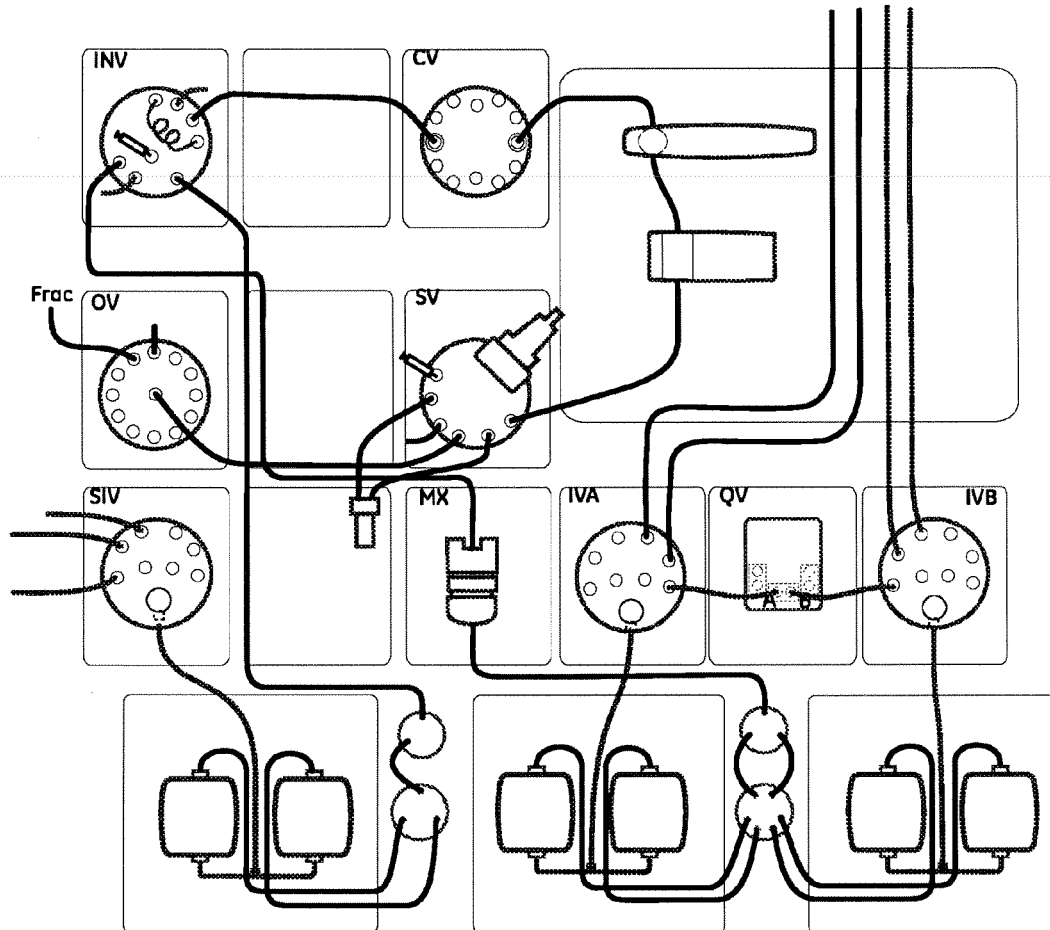


Fig. 10

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AUTOMATED FLUID HANDLING SYSTEM**CROSS-REFERENCE TO RELATED APPLICATIONS**

This application is a filing under 35 U.S.C. §371 and claims priority to international patent application number PCT/SE2010/050624 filed Jun. 4, 2010, published on Dec. 16, 2010 as WO 2010/144037, which claims priority to application number 0950431-7 filed in Sweden on Jun. 9, 2009.

BACKGROUND OF THE INVENTION

The present invention relates to the art of fluid handling system systems, and in particular to an automated fluid handling system that is highly flexible and configurable. The fluid handling system may e.g. be a liquid chromatography system, a filtration system, a chemical synthesis system or the like.

There is a large range of fluid handling systems e.g. in laboratories. Such systems comprise a number of fluid handling units, e.g. one or more pumps, valves, mixers, sensor units etc of different types. Said fluid handling units are interconnected by fluid conduits in the form of, rigid or flexible tubes or the like. Even though some systems may be designed for a specific type of application with a specific flow path, there often exists a need for flexibility and ability to alter or optimize the fluid flow path of the system. Moreover, upgrading is often restricted to specific kits provided by the manufacturer, and upgrade kits often is supplied as external add-on equipment to be arranged besides the original system, thus enlarging the foot print of the system and that need to be connected to the system both fluidically and electrically (i.e. to a system control bus or the like). Moreover, replacement of defect fluid handling units is a time consuming and delicate task.

One type of liquid handling system is liquid chromatography systems which is a standard method in laboratories, and there are a broad range of liquid chromatography systems available on the market. Common to most of the present systems is the lack of flexibility in adapting the instrument to a variety of different applications.

SUMMARY OF THE INVENTION

The object of the invention is to provide a new fluid handling system, which system overcomes one or more drawbacks of the prior art. This is achieved by the fluid handling system as defined in the independent claims.

One advantage with such a fluid handling systems is that the system may easily be upgraded without need for add-on equipment, and that the flow path may be easily optimized for new experimental setups.

Embodiments of the invention are defined in the dependent claims.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 shows one embodiment of a fluid handling system in the form of a liquid chromatography system, according to the present invention.

FIG. 2 is a schematic illustration of a housing with a liquid handling panel of the fluid handling system of FIG. 1.

FIG. 3 is a schematic illustration of the housing with the liquid handling panel of FIG. 2 with the modular components of the fluid handling system removed.

FIGS. 4a to 4d are schematic illustrations of examples of component modules of the fluid handling system removed.

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FIGS. 5a and 5b show a schematic embodiment of an automated fluid handling system.

FIG. 6 is a schematic illustration of an embodiment of a housing with a modular liquid handling panel with the modular components of the fluid handling system removed.

FIGS. 7a and 7b are schematic illustrations of an embodiment of a modular housing with a liquid handling panel with the modular components of the fluid handling system removed.

FIG. 8 is a schematic illustration of an embodiment of the system architecture of one embodiment of a fluid handling system according to the present invention.

FIG. 9 is a schematic illustration of an embodiment of a master control unit of one embodiment of a fluid handling system according to the present invention.

FIG. 10 is a schematic illustration of one embodiment of a fluidic interconnection arrangement between the modular components of the liquid handling panel for the liquid chromatography system of FIG. 1.

DETAILED DESCRIPTION OF THE INVENTION

According to one embodiment, there is provided an automated fluid handling system comprising a housing and two or more fluid handling units arranged as interchangeable modular components with an external fluidics section and an internal non fluidics section, and wherein the housing comprises a liquid handling panel with two or more of component positions for receiving said interchangeable modular components such that the external fluidics section is separated from the non fluidics section by the liquid handling panel.

According to another embodiment, there is provided a fluid handling system in the form of a liquid chromatography system comprising a housing, two or more high pressure pumps, at least one sensor unit and a plurality of fluid control valves of at least two different configurations, wherein at least the fluid control valves are arranged as interchangeable modular components and the housing comprises a liquid handling panel with a plurality of component positions for receiving said modular components.

FIG. 1 shows one embodiment of an automated fluid handling system modular in the form of a liquid chromatography system, with a plurality of interchangeable modular components arranged in a liquid handling panel wherein the reference numbers denotes:

1. Injection valve
2. Column valve with integrated pressure sensors
3. Conductivity monitor
4. UV monitor
5. Quaternary valve
6. Inlet valve B with integrated air sensor
7. System pump
8. Pressure monitor, system pump
9. Inlet valve A with integrated air sensor
10. System pump
11. Pressure monitor, sample pump
12. Sample pump
13. Rinsing system
14. Mixer with online filter
15. Sample inlet valve with integrated air sensor
16. Flow restrictor
17. pH valve
18. Outlet valve

The disclosed embodiment is supplied with three high precision pumps 7, 10, 12. There are two System pumps 7, 10, System pump A 10 and System pump B 7, and one Sample pump 12. The System pumps 7, 10 may be used individually,

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or in combination to generate isocratic or gradient elution in purification methods. The Sample pump 12 is dedicated for direct loading of sample onto a column, or for filling of sample loops.

Function of the Pumps:

Each pump module consists of two pump heads (not shown). The individual heads are identical but actuated in opposite phase to each other by individual stepper motors, controlled by a microprocessor. The two pistons and pump heads work alternately to give a continuous, low pulsation, liquid delivery. The flow rate of the two System pumps may be varied between about 0.001 ml/min and 25.000 ml/min and the maximum operating pressure is about 20 MPa. The flow rate of the Sample pump may e.g. be varied between 0.01 and 25 ml/min and according to one embodiment the maximum operating pressure is 10 MPa.

According to one embodiment, the plurality of fluid control valves of at least two different configurations are valves of rotary type. Such a motorized rotary valve may consist of a Valve head with a number of defined bores with channels to the inlet and outlet ports of the valve. The Rotary disc, mounted on the motor, has a number of defined channels. The pattern of channels of the Rotary disc together with the pattern and location of the ports of the Valve head, define the flow path and function of each type of valve. When the Rotary disc turns, the flow path in the valve changes.

One embodiment of fluid control valves are Inlet valves A and B (9, 6 respectively) that are used to select which buffers or samples to use in a run, and Sample inlet valve 15 that is located before Sample pump 12. Inlet valve A 9 1 is located before System pump A 10, Inlet valve B 6 is located before System pump B 10, and Sample inlet valve 15 is located before Sample pump 12. Inlet valve A and Inlet valve B are connected to another embodiment of a fluid control valve in the form of a Quaternary valve 5. The Quaternary valve is used for automatic buffer preparation, and for formation of quaternary gradients. The number of inlets can be increased by installing component modules with extra inlet valves. Inlet valve A and Inlet valve B enable automatic changing between different buffers and wash solutions, and can be used to generate gradients by mixing buffer A and buffer B. The air sensors integrated in Inlet valve A and Inlet valve B can be used to prevent introduction of air into the pumps and columns.

The Quaternary valve is used for automatic mixing of four different solutions. The Quaternary valve opens one inlet port at a time, and the different solutions are mixed in a Mixer 14 to form the desired buffer. The opening time in the switching valve is controlled by the system. The volume for each inlet port opening increases stepwise when the flow increases. To obtain a homogeneous buffer composition, one has to make sure to use a mixer chamber volume suitable for the flow rate of the method.

The Quaternary valve can be used to create a gradient using four different solutions simultaneously in any combination. The percentage of each solution is controlled by instructions in the method. It is possible to form gradients that changes the percentage of two, three or four solutions linearly over time. This is useful when advanced methods are developed.

The Sample inlet valve 15 enables automatic loading of different samples when using the Sample pump 12 to inject sample directly onto the column or to fill a sample loop. The Sample inlet valve has an inlet dedicated for buffer. This Buffer inlet is used in methods to fill the Sample pump with solution before sample is introduced. The Buffer inlet is also used to wash the Sample pump with buffer between runs. The air sensor integrated in the Sample inlet valve is e.g. used

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when sample is applied from a vessel onto a column by selecting Inject all sample using air sensor in the Sample application phase of a method. This function uses the Buffer inlet is used to finalize sample injection and to remove air from the Sample pump.

Still another embodiment of fluid control valve may be an Injection valve 1, which is used to direct sample onto the column. The valve enables usage of a number of different sample application techniques. A sample loop can be connected to the Injection valve and filled either automatically using the Sample pump or manually using a syringe. The sample can also be injected directly onto the column using the Sample pump.

Still another embodiment of fluid control valve may be a Column valve 2 that is used for connection of columns to the system, and to direct the flow onto the column. Up to five columns can be connected to the disclosed embodiment of said valve simultaneously. The valve also has a built-in bypass capillary that enables bypassing of connected columns.

The number of column positions can be increased by installing an extra Column valve. Both top and bottom of each column shall be connected to the Column valve. The top of the column shall be connected to one of the A ports (e.g., 1A), and the bottom of the column shall be connected to the corresponding B port (e.g., 1B). The flow direction can be set either from the top of the column to the bottom of the column, Down flow, or from the bottom of the column to the top of the column, Up flow. In the default flow path of the Column valve the columns are bypassed. Pressure monitors that measures the actual pressure over the column are integrated into the inlet and outlet ports of the Column valve.

Still another embodiment of fluid control valve may be a pH valve 17 that has an integrated flow cell where a pH electrode can be installed. This enables in-line monitoring of pH during the run. A flow restrictor is connected to the pH valve and can be included in the flow path to generate a backpressure high enough to prevent formation of air bubbles in the UV flow cell. The pH valve is used to direct the flow to the pH electrode and to the flow restrictor, or to bypass one or both.

Still another embodiment of fluid control valve may be an Outlet valve 18 that is used to direct the flow to a Fraction collector (not shown), to any of e.g. 10 outlet ports, or to waste. The number of outlets can be increased by installing an extra Outlet valve.

A Mixer 14 may e.g. be located after System pump A and System pump B and before the Injection valve. The purpose of the Mixer is to make sure that the buffers from the System pumps are mixed to give a homogenous buffer composition. The Mixer has a built-in filter that prevents impurities from entering the flow path.

To fulfil a desired purpose, with the disclosed liquid chromatography system it is possible to adapt and extend the flow path in a simple and a flexible way. Up to three extra fluid control valves or the like can be installed using the free valve positions. Dummy modules are installed in these positions at delivery. To obtain an optional flow path, it is also possible to move the standard fluid control valves to other positions. There are also two types of extra air sensors available which can be installed before Sample inlet valve or after Injection valve.

In the configuration disclosed in FIG. 1, 7 inlets are available for each inlet valve. To increase the number of inlets, an extra inlet valve can be installed which increases the number of inlets to 14 for one of the valves. This optional configuration can be convenient for example when a larger number of

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samples will be used. There is also a general type of inlet valve, Valve X, which can be used to increase the number of inlets to for example the Quaternary valve.

In the configuration disclosed in FIG. 1 with one column valve, 5 column positions are available. To increase the number of column positions to 10, an additional column valve can be installed in the instrument. An application can be to evaluate a number of different columns in method optimization.

In the configuration disclosed in FIG. 1 with one outlet valve, 10 outlet positions are available. To increase the number of outlets, one or two extra outlet valves can be connected, adding up to a total of 21 or 32 outlet positions. This optional configuration is convenient when collecting a number of large fractions outside the fraction collector.

Optional modules are easy to install in the disclosed modular liquid chromatography system. The dummy module is removed with a hexagon wrench and a bus cable is disconnected. The bus cable is connected to the optional fluid control valve or the like which is assembled in the instrument. The module is then added to the System properties in the control software. The available optional modules may e.g. be pre-configured to give the desired function. However, the function of a valve may e.g. be changed by changing the Node ID.

FIG. 2 is a schematic illustration of a housing 20 with a liquid handling panel 22 of the fluid handling system in the form of a modular liquid chromatography system 100 of FIG. 1. In FIG. 2 some components have been removed for clarity reasons. In the disclosed configuration, as disclosed in detail above, the modular liquid chromatography system 100 comprises a plurality of fluid control valves in the form of: Injection valve 1, Column valve 2, Quaternary valve 5, Inlet valve B 6, Inlet valve A 9, Sample inlet valve 15, pH valve 17, and Outlet valve 18. The chromatography system 100 further comprises UV monitor 4, System pump B 7, System pump A 10, Sample pump 12, Mixer 14, and three Dummy modules 24. According to one embodiment, all liquid handling components and sensors arranged at the liquid handling panel 22 are designed to be readily interchangeable. The interchangeability provides improved service and upgrade possibilities and also a possibility to customize the positions of the respective liquid handling components, such as the fluid control valves, e.g. in order to optimize the fluid path for a specific experimental setup. As is illustrated in FIG. 2, there are three large component positions e.g. for pump modules, one UV-sensor position and 9 standard component positions, e.g. for fluid control valves or the like. The component positions are given a standardized size and shape to provide simple interchangeability. According to one embodiment, each modular component is retained in a mating component position by a single screw, and it is connected to the master control unit by a single bus cable providing both communication and system power to each component. FIG. 3 is a schematic illustration of the housing with the liquid handling panel of FIG. 2 with the modular components of the liquid chromatography system removed.

FIGS. 4a to 4d are schematic illustrations of examples of fluid handling units in the form of modular component of the fluid handling system removed. FIG. 4a shows a standard interchangeable modular component 26, e.g. a fluid control valve or the like. The standard component module 26 comprises a panel member 28, an external fluidics section 30 and an internal non-fluidics section 32. According to one embodiment, the panel member 28 essentially separates the fluidics in the external fluidics section 30 from electronics and control means in the internal non-fluidics section 32.

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FIG. 4b shows a Dummy module 24, which is intended to be placed in non used standard component positions. In the disclosed embodiment, the Dummy modules are provided with mounting grooves for attachment of accessories to the system. In the disclosed embodiment the dummy module is shown as a panel member 28 without any internal section FIGS. 4c and 4d shows a pump module and an UV-module, respectively, each having an external fluidics section 30 and an internal non-fluidics section 32.

As is disclosed in FIGS. 4a to 4d, the interchangeable modular components 26 comprises a panel member arranged to separate the fluidics section from the non fluidics section and for attachment to a component position in the liquid handling panel. Said panel attachment member may be arranged so that all fluid connections of said modular component are arranged on a wet side of the panel attachment member separating them from electrical components that are arranged on a dry side thereof, hence providing a high degree of liquid resistance at the external part of the fluid handling panel, and so that the liquid resistance requirements for the internal sections may be somewhat lightened. According to one embodiment, the interchangeable modular components are sealed against the liquid handling panel by a sealing member. According to another embodiment, not shown, the modular component does not comprise any panel member, but there is provided a suitable sealing arrangement between the component position openings of the liquid handling panel and the external surface of the interchangeable modular components 26. In the disclosed embodiments, the component position openings of the liquid handling panel and the interchangeable modular components 26 are shown to have an essentially rectangular cross sectional shape, but other shapes may be equally applicable.

According to one embodiment, there is provided a general fluid handling system comprising a housing and two or more fluid handling units arranged as interchangeable modular components as is schematically disclosed in FIG. 5a. As discussed above such a system may be configured for essentially any type of automated liquid handling operations provided that suitable fluid handling units are provided as interchangeable modular components for the system. According to one embodiment there is provided an automated fluid handling system comprising at least one fluid pump, at least one sensor unit and two or more fluid control valves of at least two different configurations, wherein at least the fluid control valves are arranged as interchangeable modular components.

The liquid handling panel 22 of the fluid handling system may e.g. be designed in any suitable manner to allow the modular components to be arranged in an efficient manner.

FIGS. 5a and 5b shows a schematic embodiment of an automated fluid handling system wherein the housing 20 comprises an internal climate panel 29 arranged at a distance behind the liquid handling panel 22 defining an air inlet compartment 35 and air outlet compartment 37 in the housing 20, the climate panel 29 being provided with complementary component positions 39 for receiving the internal non fluidics section 32 of the interchangeable modular components 26, and wherein the non-fluidics section 32 of at least one interchangeable modular component is provided with one or more air inlet openings 31 located in the air inlet compartment 35 and one or more air outlet openings 33 located in the air outlet compartment 37 when the interchangeable modular component arranged in position in the component position. FIG. 5b shows the fluid handling system of FIG. 5a in a schematic cross sectional view. As is indicated by inlet vent 41 and outlet vent 43, air for cooling interchangeable modular components 26 provided with air inlet and outlet openings 31, 33 is pref-

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erably arranged to enter the air inlet compartment 35 at a distance from the outlet vent 43 in order to avoid recirculation of air. The air circulation in the system may be achieved by a system cooling unit (not shown) providing a flow of air from the air inlet compartment 35 to the air outlet compartment 37, through the at least one interchangeable modular component 26. Alternatively, the at least one interchangeable modular component 26 is provided with a local cooling unit (not shown) providing a flow of air from the air inlet compartment 35 to the air outlet compartment 37. As is indicated, the complementary component positions 39 are arranged to provide a relatively air flow tight fit with respect to the internal non fluidics section 32 of the interchangeable modular components 26, and according to one embodiment, this may be achieved by a sealing arrangement. In FIG. 5b, there is shown a sealing member 45 for sealing the interchangeable modular components 26 with respect to the liquid handling panel 22, as discussed above. Other sealing member arrangements may be envisaged by a person skilled in the art. According to one embodiment, fluids are strictly restricted to the fluidics section 30 of the interchangeable modular component 26, but in alternative embodiments, only fluid connections are restricted to the fluidics section 30 allowing fluid to "cross" the fluid handling panel inside the non-fluidics section 30 of the interchangeable modular component 26.

In FIG. 5b there is further shown a master control unit 40 and buss connectors 42 for connecting the interchangeable modular components 26 to the master control unit 40. According to one embodiment, the component positions including the buss connectors 42 and the interchangeable modular components 26 are of plug and play configuration with respect to each other.

FIG. 6 is a schematic illustration of an embodiment of a housing 20 with a modular liquid handling panel 22 with the modular components of the liquid chromatography system removed. In the disclosed embodiment, also the layout of the liquid handling panel 22 is configurable by means of two interchangeable panel sections 34 which may be selected in accordance with the desired layout of the system. In FIG. 6 two different layouts of the interchangeable panel sections are disclosed, but the layout may include any suitable configuration.

FIGS. 7a and 7b are schematic illustrations of an embodiment of a modular housing with a liquid handling panel with the modular components of the liquid chromatography system removed. In the disclosed embodiment, the modular housing is comprised of a main housing 36 that comprises the master control unit including power supply and climate control for the whole housing, two expansion housing modules 38 and a side member 40. This approach provides very flexible expansion possibilities for the chromatography system, while preserving the benefits of a single master control unit including power supply and climate control.

FIG. 8 is a schematic illustration of an embodiment of the system architecture of one embodiment of a modular liquid chromatography system according to the present invention. As mentioned above, the chromatography system may comprise a master control unit 40 arranged to communicate with all modular components e.g. 1-26, over a system bus 42 such as a CAN-bus or the like. In one embodiment, each modular component is provided with a dedicated CPU unit allowing the component to independently perform operations in response to instructions over the BUS 42. In order to minimize the number of connectors to be attached to each modular component, the bus 42 further comprises power feed for the modular components. The Bus 42 may be connected to any suitable number of modular components arranged in the

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housing 20, but also to one or more modular components 44 outside of the housing 20 or the like. As is mentioned briefly above, the master control unit may further be arranged to control the climate in the housing. In addition to the disclosed modular components, other components of the chromatography system, e.g. a fraction collector or the like, may be arranged in the housing and the controlled climate therein.

According to one embodiment, different component modules are automatically identified by the master control unit, whereby they may be moved essentially freely between different positions. Moreover, the master control unit may be arranged to provide said information to Chromatography control software whereby experimental setup and planning may be performed. In one embodiment, the control system may be arranged to provide an optimized layout of the component modules with respect to the present layout of the liquid handling panel and available component modules for a specific experimental setup.

According to one embodiment, the interchangeable panel sections 34 of FIG. 5 and the expansion housing modules 38 of FIGS. 6a and 6b may be provided with means for automatic detection of the same to allow automatic configuration of the system by the master control unit 40. In one embodiment, each interchangeable panel section 34 and expansion housing module 38 comprises a hub (not shown) for connection to the system bus 42 in order to expand the system bus 42 network to the number of component modules in each interchangeable panel section 34 or expansion housing module 38.

FIG. 9 is a schematic illustration of an embodiment of a master control unit of one embodiment of a modular liquid chromatography system according to the present invention. The master control unit 40 comprises a system controller 46 for communicating with internal and external components and control computers (not shown) etc. According to one embodiment, the system controller comprises a suitable CPU 48, a bus controller 52, an external communications controller 50, such as a LAN unit, and a storage device 54. The bus controller 52 is providing communication with the component modules. The master control unit may further comprise a Power supply 56 and a climate controller 58 arranged to keep the internal climate in the housing 20 at a predetermined level as discussed above.

FIG. 10 is a schematic illustration of one embodiment of a fluidic interconnection arrangement between the modular components of the liquid handling panel. Taking into account the complexity of the disclosed interconnection arrangement, the benefit of optimizing the fluid paths in alternative configurations of the system becomes evident. The task of optimizing the fluid paths may e.g. be performed to reduce the total length/volume of the fluid paths/tubing arranged to interconnect the different component modules in the system. Alternatively the optimization may be performed to minimize the length/volume of one or more specific fluid paths, such as the sample output path from the column to the fraction collector, in order to minimize dispersion of the fractionized sample.

The invention being thus described, it will be obvious that the same may be varied in many ways. Such variations are not to be regarded as a departure from the spirit and scope of the invention, and all such modifications as would be obvious to one skilled in the art are intended to be included within the scope of the following claims.

What is claimed is:

1. Automated fluid handling system comprising a housing and two or more interchangeable fluid handling units the housing comprising a liquid handling panel including two or more component positions for receiving said interchangeable

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units, wherein said units are arranged as interchangeable modular components, and include:

- a fluidics section;
- a non fluidics section comprising electronics or electrical components or control means; and
- a panel member arranged to separate the fluidics section from the non fluidics section and for attachment of the modular component to a component position of the liquid handling panel,

and wherein the two or more component positions of the liquid handling panel are arranged for attachment of the panel members such that said respective fluidics sections are external to the housing and said respective non fluidics sections are internal to the housing.

2. The fluid handling system of claim 1, wherein the interchangeable modular components are sealed against the liquid handling panel by a sealing member.

3. The fluid handling system of claim 1, comprising a master control unit wherein the interchangeable modular components are connected to the master control unit by a system bus providing electrical communication to each interchangeable modular component.

4. The fluid handling system of claim 1, wherein all interchangeable modular components are of same size.

5. The fluid handling system of claim 1, wherein the interchangeable modular components are of two or more sizes.

6. The fluid handling system of claim 1, comprising at least one fluid pump, at least one sensor unit and two or more fluid control valves of at least two different configurations, wherein at least the fluid control valves comprise said interchangeable modular components.

7. The fluid handling system of claim 3, wherein the master control unit comprises a system climate controller for controlling the climate in the housing and the interchangeable modular components.

8. The fluid handling system of claim 1, wherein the housing comprises an internal climate panel arranged spaced from the liquid handling panel within the housing, said internal climate panel defining on one side an air inlet compartment and defining on an opposing side an air outlet compartment in the housing, the climate panel being provided with complementary component positions for receiving the internal non fluidics section of the interchangeable modular components, and wherein the non-fluidics section of at least one interchangeable modular component is provided with one or more air inlet openings located in the air inlet compartment and one or more air outlet openings located in the air outlet compartment when the interchangeable modular component is arranged in position in the component position.

9. The fluid handling system of claim 8, further comprising a system cooling unit providing a flow of air from the air inlet compartment to the air outlet compartment, through said at least one interchangeable modular component.

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10. The fluid handling system of claim 8, wherein said at least one interchangeable modular component is provided with a local cooling unit providing a flow of air from the air inlet compartment to the air outlet compartment.

11. The fluid handling system of claim 1, wherein the system is a liquid chromatography system arranged to provide a controlled fluid flow through a chromatography column.

12. The fluid handling system of claim 1, wherein the system is a liquid filtration system.

13. The fluid handling system of claim 1, wherein the system is a chemical synthesis system.

14. The fluid handling system according to claim 1 wherein the system further comprises at least one expansion housing module for accommodating additional interchangeable modular components.

15. The fluid handling system according to claim 14, further including means for automatic detection of said module to allow automatic configuration of the system by a master control unit.

16. A liquid chromatography system arranged to provide a controlled fluid flow through a chromatography column, the system comprising a housing and two or more interchangeable fluid handling units, the housing comprising a liquid handling panel including two or more component positions for receiving said interchangeable units, wherein said units are arranged as interchangeable modular components, and include:

- a fluidics section;
- a non fluidics section in turn comprising electronics or electrical components or control means; and
- a panel member arranged to separate the fluidics section from the non fluidics section and for attachment of the modular component to a component position of the liquid handling panel,

and wherein the liquid handling panel of the housing and the panel members are arranged such that the fluidics sections are external to the housing and respective non fluidics sections are internal to the housing.

17. The liquid chromatography system according to claim 16, wherein the interchangeable modular components include at least one of: an injection valve; a column valve with integrated pressure sensors; a conductivity monitor; a UV monitor; a quaternary valve; an inlet valve with integrated air sensor; a system pump; a pump pressure monitor; an inlet valve with integrated air sensor; a rising valve; a mixer; a filter; a sample inlet valve; a flow restrictor; a pH valve; an outlet valve; and a dummy component.

18. The liquid chromatography system according to claim 17, wherein said modular components are interconnected fluidically on the external side of the panel.

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